

Passive smoking by self report and serum cotinine and the prevalence of respiratory and coronary heart disease in the Scottish heart health study

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Abstract

Study objective – To explore the relationship between self reported environmental tobacco smoke exposure (or passive smoking), the serum cotinine concentration, and evidence of respiratory or coronary disease in men and women who have never smoked.

Design – Cross sectional random population survey identifying disease markers and relating them to measures of passive smoking. Disease markers were previous medical diagnoses, response to standard symptom questionnaires, and electrocardiographic signs.

Setting – Samples of men and women aged 40–59 years drawn from general practitioner lists in 22 local government districts of Scotland, between 1984 and 1986.

Participants – A total of 786 men and 1492 women who reported never having smoked tobacco, and who had serum cotinine concentrations below 17.5 ng/ml, the cut off point for smoking “deceivers”, took part.

Results – Fewer than one third of never smokers reported no recent exposure to environmental tobacco smoke and the same proportion had no detectable cotinine. Women had lower cotinine values than men but reported more exposure to smoke. The correlation between the measures of exposure was poor. Self reported exposure showed strong, statistically significant, dose response relationships with respiratory symptoms and with the coronary disease markers. These relationships were weak or absent for serum cotinine, except for diagnosed coronary heart disease. Here the dose response gradient was as strong as that for self report, with an odds ratio of 2.7 (95% CI 1.3, 5.6) for the highest v the lowest exposure group, adjusted for age, housing tenure, total cholesterol, and blood pressure, and not explained by fibrinogen.

Conclusions – The validity of different measures of tobacco smoke exposure needs further investigation. The gradient of diagnosed coronary heart disease with both self reported exposure and serum cotinine was, however, surprisingly strong, statistically significant, and unexplained by other factors. These findings reinforce

current policies to limit passive tobacco smoke exposure.

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Because of the low dose levels involved, investigation of the long term effects of passive exposure to tobacco smoke in non-smokers stretches epidemiological studies to their limits. If the excess risk over non-exposure is small, it may be explained by confounding factors, or the inclusion of furtive smokers,¹ if it is large, it may lack a plausible biological mechanism. Opinion is divided on whether evidence on passive smoking in relation to coronary heart disease (CHD) is unconvincing,² sufficiently suggestive that it cannot be ignored,³ or proving that thousands of deaths a year are caused by it.^{4–6} The issue is of considerable importance to the public health.

Most studies of passive smoking have been done without biochemical validation to grade the exposure and exclude smoking deceivers. In a large cross sectional population survey, the Scottish heart health study (SHHS), we asked non-smokers about recent exposure to tobacco smoke and also measured their serum cotinine.⁷ We related these to questionnaire and electrocardiographic evidence of disease.

Subjects and methods

SURVEY METHOD

Men and women aged 40–59 years were recruited by random sampling from general practitioner lists between 1984 and 1986.⁸ Each was sent a “personal health record” to complete and a clinic appointment. The former included the standard Rose angina and possible infarction questionnaire; the Medical Research Council cough and phlegm questionnaire; questions on prior medical diagnoses, on current and former consumption of cigarette, pipe, or cigar tobacco; and the question, “Have you been exposed to tobacco smoke from someone else in the last three days?” with possible answers of: “1 – yes, a lot; 2 – yes, some; 3 – yes, a little; 4 – none at all”.

Relevant clinic procedures included checking the questionnaire, a 12 lead electrocardiogram, and venepuncture. Blood analyses included serum cholesterol, serum cotinine, assayed by

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Table 1 Distribution of men and women by (A) self reported exposure to tobacco smoke over three days and by (B) serum cotinine group

	(A) Self reported exposure group				All	(B) Serum cotinine group			
	None	Little	Some	A lot		I	II	III	IV
Men									
No	190	347	176	73	786	208	241	204	133
(%)	(24)	(44)	(22)	(9)	(100)	(27)	(31)	(26)	(17)
Women									
No	428	467	378	219	1492	548	433	349	162
(%)	(29)	(31)	(25)	(15)	(100)	(37)	(29)	(24)	(11)
All									
No	618	824	554	292	2278	756	674	553	295
(%)	(27)	(36)	(24)	(13)	(100)	(33)	(30)	(24)	(13)

Cotinine groups: I no detectable cotinine; II >0–1.05 ng/ml; III 1.06–3.97 ng/ml; IV 3.98–17.49 ng/ml.

the method of Feyerabend,⁹ and plasma fibrinogen.¹⁰

DEFINITION OF PASSIVE SMOKING POPULATION AND GROUPINGS

Excluded from this analysis is anyone who admitted to active tobacco smoking currently or in the past, or who had no serum cotinine measurement, or who had a reading at or above 17.5 ng/ml, our threshold for possible smoking deceivers.¹¹ Replies to the question on passive smoking produced four unequal groups. Cut points were chosen in the serum cotinine results to give groups which corresponded in size to their questionnaire equivalents.

DEFINITION OF DISEASE CATEGORIES

Chronic cough was cough first thing in the morning or at any time during the day, for as much as three months each year.

Chronic phlegm was bringing up of phlegm first thing in the morning or at any time during the day, for as much as three months each year.

Questionnaire angina was chest discomfort on exertion relieved by rest, in those without diagnosed coronary heart disease.

Undiagnosed CHD (coronary heart disease) included questionnaire angina, or questionnaire "possible myocardial infarction"; or electrocardiographic findings of myocardial infarction or ischaemia (Minnesota codes for Q and QS waves 1.1–1.3, ST depression 4.1–4.4, T inversion and flattening 5.1–5.3 or left bundle branch block 7.1)¹² in those without diagnosed coronary heart disease.

Diagnosed CHD was the reporting of a medical diagnosis of angina, myocardial infarction, coronary thrombosis, or a heart attack.

All CHD was the preceding two categories combined.

STATISTICAL METHODS

The relationship of the self report and cotinine grouping to the different diseases was examined by logistic regression analysis using GLIM.¹³ Prevalence odds ratios were calculated relative to the least exposure group, with 95% confidence limits. Odds ratios for coronary heart disease were adjusted for age, housing tenure, serum cholesterol, and diastolic blood pressure, possible confounding factors identified in previous analyses,¹⁴ while those for respiratory disease were adjusted for age and housing tenure.

Results

POPULATION FOR STUDY

The SHHS response rate was 74%, yielding 5123 men and 5236 women. Active cigarette smoking involved 38% in both sexes. More men were pipe, cigar, or ex-smokers. After excluding smokers, people with no cotinine result,⁷ and 21 men and 28 women with cotinine readings at or above 17.5 ng/ml¹¹ (possible deceivers) 786 men and 1492 women allegedly, never smokers were left. These subjects figure in subsequent analyses, unless missing data or specific definitions exclude them.

PASSIVE SMOKING GROUPS BY THE TWO METHODS OF DEFINITION

The passive smoking groups, defined by self report are shown in table 1(A), and by serum cotinine in 1(B). Only 27% reported no exposure to tobacco smoke, while 13% reported a lot. The distribution across the four groups was different in the two sexes ($\chi^2=47$, $p<0.0001$), more women than men reported both no exposure and a lot of exposure. Cotinine readings of zero accounted for 33% of never smokers (group I). Subsequent cut off points were designed to match the self report groups. Group II had readings from 0.01 ng/ml to 1.05 ng/ml, group III 1.06–3.97 ng/ml, and group IV 3.98 to 17.49 ng/ml. The sexes differed in serum cotinine groups ($\chi^2=34$, $p<0.0001$) in that women scored lower than men. Nonetheless there were no important differences or interactions in relation to sex in subsequent analyses and the results are combined.

The joint distribution by passive smoking classes is shown in table 2. Agreement means

Table 2 Distribution across self reported exposure and serum cotinine groups (sexes combined)

Self report group		Serum cotinine group				All
		I	II	III	IV	
None	No	285	194	103	36	618
	O/E	1.39	1.06	0.69	0.45	
Little	No	274	251	199	90	814
	O/E	1.01	1.04	1.00	0.86	
Some	No	140	152	167	95	554
	O/E	0.76	0.93	1.25	1.32	
A lot	No	57	77	84	74	292
	O/E	0.59	0.89	1.19	1.96	
All	No	756	674	553	295	2278

No is the observed number in each subgroup, and O/E the ratio between the observed number and that expected in the subgroup if there were no association between self report and serum cotinine.

Table 3 Disease prevalence and odds ratio trends across categories of passive smoking defined by self reported exposure and by serum cotinine

	All	Reported exposure group				Serum cotinine group			
		None	Little	Some	A lot	I	II	III	IV
<i>Chronic cough</i>									
No positive	121	27	36	30	28	39	40	25	17
Prevalence (%)	(5.5)	(4.5)	(4.6)	(5.5)	(9.9)	(5.3)	(6.1)	(4.7)	(5.9)
Odds ratio*		1.0	1.0	1.2	2.3	1.0	1.2	0.8	1.1
(95% CI)			(0.6, 1.7)	(0.7, 2.1)	(1.3, 3.9)		(0.7, 1.8)	(0.5, 1.4)	(0.6, 1.9)
<i>Chronic phlegm</i>									
No positive	142	32	38	40	32	42	48	33	19
Prevalence (%)	(6.4)	(5.3)	(4.8)	(7.4)	(11.3)	(5.7)	(7.3)	(6.1)	(6.6)
Odds ratio*		1.0	0.9	1.4	2.3	1.0	1.3	1.1	1.2
(95% CI)			(0.6, 1.5)	(0.9, 2.3)	(1.4, 3.9)		(0.9, 2.0)	(0.7, 1.7)	(0.7, 2.0)
<i>Questionnaire angina</i>									
No positive	104	20	33	30	21	35	29	28	12
Prevalence (%)	(5.6)	(3.9)	(4.9)	(6.8)	(8.9)	(5.6)	(5.1)	(6.4)	(5.0)
Odds ratio†		1.0	1.3	1.6	2.1	1.0	0.9	1.0	0.8
(95% CI)			(0.7, 2.3)	(0.9, 2.8)	(1.1, 3.9)		(0.5, 1.4)	(0.6, 1.7)	(0.4, 1.5)
<i>Undiagnosed CHD</i>									
No positive	358	83	125	98	52	114	96	101	47
Prevalence (%)	(16.8)	(14.3)	(16.3)	(19.1)	(19.5)	(16.1)	(15.2)	(19.7)	(17.0)
Odds ratio†		1.0	1.2	1.4	1.4	1.0	0.9	1.2	1.0
(95% CI)			(0.9, 1.6)	(1.0, 1.9)	(0.9, 2.0)		(0.7, 1.2)	(0.9, 1.6)	(0.7, 1.4)
<i>Diagnosed CHD</i>									
No positive	70	16	16	21	17	15	20	19	16
Prevalence (%)	(3.3)	(2.8)	(2.1)	(4.1)	(6.4)	(2.1)	(3.2)	(3.7)	(5.8)
Odds ratio†		1.0	0.8	1.6	2.4	1.0	1.5	1.7	2.7
(95% CI)			(0.4, 1.7)	(0.8, 3.1)	(1.1, 4.8)		(0.8, 3.0)	(0.8, 3.3)	(1.3, 5.6)
<i>All CHD</i>									
No positive	428	99	141	119	69	129	116	120	63
Prevalence (%)	(20.1)	(17.0)	(18.4)	(23.2)	(25.9)	(18.2)	(18.4)	(23.4)	(22.8)
Odds ratio†		1.0	1.2	1.5	1.6	1.0	1.0	1.3	1.2
(95% CI)			(0.9, 1.5)	(1.1, 2.0)	(1.1, 2.4)		(0.8, 1.3)	(1.0, 1.7)	(0.9, 1.7)
Overall no	2278	618	824	554	292	756	674	553	295
Plasma fibrinogen (g/l)†	2.21	2.23	2.21	2.20	2.26	2.19	2.21	2.26	2.23
Standard error	0.02	0.03	0.03	0.03	0.04	0.03	0.03	0.03	0.04

* Adjusted for age and housing tenure;

† Adjusted for age, housing tenure, and also for cholesterol and diastolic blood pressure.

greater numbers in cells where criteria are congruent. This happens, but not enough to make one measure a reliable predictor of the other. Cells with congruent categories contain about twice the number expected, while incongruent cells contain half the number expected if there were no association.

PREVALENCE OF DISEASE AND ODDS RATIO BY DEGREE OF PASSIVE SMOKING

Table 3 shows the prevalence and odds ratios for respiratory and coronary heart disease first for self reported passive smoking, and then for serum cotinine groups. *Chronic cough* and *chronic phlegm* each occur in about 6% of the population. The prevalence is twice as high in those reporting exposure to "a lot" of tobacco smoke as "none". The odds ratios are significantly raised, with 95% confidence limits above 1.00. Adjustment for age and housing tenure had little effect. *Questionnaire angina* shows a clear gradient of prevalence with increasing self reported exposure, with the odds ratio in the highest exposure group of 2.1, after added adjustment for cholesterol and diastolic blood pressure. The 358 cases of *undiagnosed CHD* also show a gradient in odds ratios but this does not reach statistical significance. With smaller numbers, *diagnosed CHD* shows a significantly raised odds ratio in the high exposure group. When *all CHD* categories are combined there is a steady, significant gradient.

Results for serum cotinine do not corroborate self report. The raised odds ratios and statistical significance disappear with respiratory symptoms, and *questionnaire angina*. When *all CHD*

categories are combined, the odds ratio in group IV is lower than that in the comparable "a lot" group and it does not reach statistical significance after adjustment, although this is reached if groups III and IV are combined. In *diagnosed CHD* the gradient is stronger than for self report. The odds ratio for group IV is significantly high, and this is also true for groups III and IV combined.

Plasma fibrinogen findings do not explain the raised odds ratios for coronary heart disease. Any possible gradient by passive smoking group is tiny (table 3). The correlation coefficient between plasma fibrinogen and serum cotinine in never smokers before adjustment was 0.038. After adjustment for the factors listed it was 0.033, and insignificant. By contrast with the gradient shown, the mean fibrinogen in active tobacco smokers in the SHHS was 2.46 g/l, and in ex-smokers 2.25 g/l, after adjustment for the same factors.

Discussion

TOBACCO SMOKE EXPOSURE IN THE GENERAL POPULATION

Only one third of never smokers had no recent exposure to tobacco smoke by either method of assessment, or one sixth if they are combined (table 2). This implies that only 5–10% of the whole SHHS population, typical of Scotland in 1984–6, had neither smoked in the past or been passively exposed in the last few days. This estimate may be too low if nicotine in food affects the serum cotinine,^{15 16} or too high, as assay methods are not improved and more sensitive^{16 17} than the one used for the SHHS.⁹

DISAGREEMENT BETWEEN SELF REPORTED DEGREE OF EXPOSURE AND SERUM COTININE MEASUREMENTS

Their poor correlation with each other and disparate association with disease undermine the validity of the two measures of passive smoking. We doubt that either measure is more ephemeral as exposure is usually chronic, and responses and serum cotinine concentrations did not fluctuate much by day of the week. Self report concerned exposure during three days, and the half life of serum cotinine in non-smokers can be as much as 40 hours.¹⁸

It is claimed that cotinine is a poor measure of passive smoking¹⁵ because of individual variation in nicotine metabolism¹⁹ and traces of nicotine in foodstuffs.¹⁶ The latter claims do not seem to have been substantiated in human data; our analyses from the SHHS refute the claim that heavy tea consumption would interfere with the relationship between passive smoking and serum cotinine.²⁰ The four cotinine groups cover a huge range of readings so a degree of variation in metabolism and imprecision in the cotinine assay⁹ should not invalidate the broad ranking. Amalgamation into two rather than four groups does not change the study findings.

Self report could be biased. Our cigarette smoking men and women ran similar serum cotinine concentrations for the same cigarette consumption,⁷ so the lower cotinine in women shown here for higher self reported exposure suggests a possible bias in reporting of the latter. Those study participants with hyper-reactive bronchial mucosa might react to tobacco smoke by exaggerating exposure (questionnaire positive) and avoiding it (cotinine negative). Twenty four of 188 of those complaining of cough or phlegm were on treatment for asthma with bronchodilators or corticosteroids or both. Participants with symptoms of disease might exaggerate exposure because they had heard of an association. This is plausible in the middle 1980s for respiratory disease, but less so for diagnosed coronary heart disease and implausible for its undiagnosed manifestations. Table 3 shows paradoxically that it is the undiagnosed group which show a greater odds ratio for self report than for cotinine, whereas the diagnosed group shows the opposite. We cannot therefore explain the discrepancies between self report and serum cotinine, and consider that more needs to be done on the validation of these measures as passive smoking becomes of increasing public health and medico-legal interest. If self reported exposure is unreliable it still suggests that those with early markers of disease tolerate smoke exposure badly.

PASSIVE SMOKING AND CORONARY HEART DISEASE

Self reported exposure shows a significant gradient for all categories of coronary heart disease, considered separately or together (table 3). If exposure is assessed using cotinine only *diagnosed CHD* shows a significantly high odds ratio in the highest exposure group after ad-

justment whereas *all CHD* (to which it contributes) shows a significant excess only if groups III and IV are combined. *Undiagnosed CHD* shows slight evidence of a gradient but *questionnaire angina* shows none at all. A possible explanation for the greater gradient with *diagnosed CHD* is its greater specificity. The *undiagnosed* category includes more mild and asymptomatic cases, but it is diluted with false positives.

The odds ratios of interest are those for *diagnosed CHD* and *all CHD*. After adjustment, the odds ratios for the top group are 2.4 and 1.6 (see table 3) for self report, and 2.7 and 1.2 for cotinine. Odds ratios in published studies of heart disease and passive smoking show considerable variation, ranging from 0.97 to 3.0, but some of these lack precision because of small numbers.⁶ The Midspan study, also from Scotland, reported a rate ratio of 2.01, with 95% confidence limits of 1.21, 3.35, based on a 12 year follow up.²¹ Our prevalence results are consistent. If the odds ratio is high in this region, the question arises as to whether the increase is consequent on misclassification, related directly and causally to passive smoking itself, or to lifestyle and other factors associated with it, or to both.

The mechanism by which active smoking causes heart disease is not known, although some authors, and our own analyses, suggest a strong relationship with fibrinogen.^{10, 22} Fibrinogen values show a tiny gradient (table 3), inadequate to explain the odds ratios we found. We have excluded current smoking deceivers by our cotinine barrier, but cannot exclude inaccurate questionnaire responses on past smoking history or occasional smoking. However, the numbers of deceivers involved, and their excess risk, would need to be very considerable to produce the odds ratios we have found, nor would we expect concealed ex-smokers to necessarily expose themselves currently to high levels of passive smoking.

We have adjusted for other confounding factors for coronary heart disease such as coronary risk factors and social status¹⁴ before presenting these odds ratios. It is unlikely that we have corrected for everything, but we would not expect confounding factors to account for such a large residual effect.

We have therefore found a significantly increased prevalence of diagnosed coronary heart disease, associated with environmental tobacco smoke, otherwise known as passive smoking, which we cannot explain. Although unexplained, these findings tend to support current attempts to minimise passive exposure to tobacco smoke.

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